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Exposure and Human Health Reassessment of 2,3,7,8-Tetrachlorodibenzo-p-Dioxin (TCDD) and Related Compounds

Addendum to Part I: Estimating Exposure to Dioxin-Like Compounds

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Following are passages which amend the current versions of Volumes 2, 3, and 4 of Part 1: Estimating Exposure to Dioxin-Like Compounds. These passages reflect the most current collection of data, analysis, and in some cases, plans for important changes based on data analysis currently underway. Each passage will identify what Volume, Chapter, and Section that is being changed. In some cases, actual replacement text along with references and tables are offered. In other cases, there is a qualitative discussion of analysis currently underway. It should be understood that the changes outlined below will reverberate throughout the Volumes. These additions, and all necessary changes, are being melded into working versions of the Exposure Documents within EPA, and they will become part of the final versions of the documents.

The following is to be placed in Volume 2: Sources of Dioxin-Like Compounds in the United States, Chapter 1: Introduction and Overview of Sources, Section 1.5, page 1-13.
Insert in second finding, end of paragraph.

EPA recognizes that for many incineration and combustion sources, the trend has been a further decline in dioxin emissions from the 1995 estimate presented here. EPA hopes to conduct periodic revisions to the Source Inventory in the future to track changes in environmental releases over time.

Efforts are underway to update sections in Volume III. Properties, Environmental Levels, and Background Exposures that involve concentrations in dioxin-like compounds in food products. The following describes planned changes. These changes will impact discussions in Chapter 3. Levels of CDD, CDF, and PCB Congeners in Environmental Media and Food, Chapter 4. Human Exposures to CDD, CDF, and PCB Congeners, and Chapter 5. Potentially Elevated Exposures.

1. Egg data

The current data on CDD/CDF levels in eggs are limited compared to the meat and dairy products. EPA is currently reviewing some unpublished egg data and, if found acceptable, will incorporate them into this report before it becomes final. Based on a preliminary analysis, it does not appear that these new data will significantly change the current background TEQ estimate for eggs, but they should provide additional support and strengthen the confidence in the estimate. Given the low egg consumption rate, total TEQ intakes will also not be significantly affected.

2. Fish Data

The current data on levels of dioxin-like compounds in fish are limited compared to other meats and dairy products. EPA hopes to receive additional data over the next few months which can be incorporated into this report before it becomes final. It is not clear if these new data will significantly change the current estimates. Issues specific to the major fish classes are discussed below:

The current document uses the National Bioaccumulation Study for deriving estimates of dioxin-like compounds (specifically CDD/CDF) levels for freshwater/estuarine fish. This study consisted of a national sampling of fish from fresh and estuarine water bodies in the US and included a relatively large number of observations from background sites. However, it has two limitations for current purposes. First, it is somewhat dated since the sample collections and the chemical analysis were made in the late 1980's. Second, the freshwater fish collected in this study were all caught in the wild and may not be appropriately representative of the species in the commercial fish supply. For example, no farm raised fish were sampled and they represent almost all of the commercial freshwater fish commonly consumed. Over the next few months, EPA intends to evaluate the possibility of using the National Bioaccumulation Study and additional data on wild caught fish to derive intake estimates of dioxin-like compounds for recreational fishers and to seek new data specific to commercial fish to derive intake estimates for the general population. Another issue for this fish class, is to consider dividing it into fin fish and shell fish categories as was done for the marine fish. The dioxin levels in these categories may be different and consumption rates specific to each category are available.

Very few studies were found describing levels of dioxin-like compounds in the commercial marine fish consumed in the U.S. The currently used data on dioxin-like compounds do not represent some of the most highly consumed marine species in the U.S. (e.g., tuna, cod, salmon, etc.). EPA will continue to seek new data, but new surveys are likely to be needed to improve our understanding of levels of dioxin-like compounds in fish.

The following subsection will appear in Volume III. Properties, Environmental Levels, and Background Exposures, Section 4.2. Levels of Dioxin-Like Compounds in Human Tissues. Included here are studies which were described in bold in Section 4.2.1; they were highlighted as not being available in time for inclusion in the overall congener profile. The new section will be numbered as Section 4.2.3. and will form the basis of the finding for current levels of dioxin-like compounds in Americans in background conditions. As such, text changes will be required for other subsections in 4.2, other sections in Chapter 4, and other changes throughout Volume 3, which reflect this conclusion.

4.2.3. The Blood Studies of the CDC Collaboration

The Centers for Disease Control (CDC) has compiled data on blood concentrations of dioxins, furans, and coplanar PCBs from individuals in the United States with no known exposures to dioxins. These data come from site-specific studies (with permission from principle investigators in those studies), and CDC has provided the laboratory analyses of all the blood samples. All the samples were collected between 1995 and 1997. There are a total of 316 individuals included in their compilation from six locations: 1) Manchester, Missouri (n = 61), 2) Times Beach, Missouri (n = 67), 3) Jacksonville, Arkansas (n = 57), 4) Oregon (n = 9), 5) Wisconsin (n = 93), and 6) North Carolina (n=29). CDC is preparing manuscripts for peer literature publication of statistical summaries and interpretations of this data. They have provided EPA with an overall statistical summary of the congener-specific and overall TEQ results from this compilation (Patterson, 2000), and those results will be described shortly. EPA judges these data to be the best representation of current background concentrations of dioxin-like compounds in the blood of US citizens, for these reasons: 1) all individuals were evaluated by the CDC analysis group as appropriately representing US background conditions and EPA concurs with this evaluation - that is, all individuals were judged to be exposed only through background exposures, including inhalation of background ambient air (i.e., not impacted by nearby high dioxin stack emitters), consumption of animal food products not known or expected to be contaminated, no occupational exposures, and so on, 2) the blood was analyzed using a consistent, high resolution, mass spectrometry state-of-the-art protocol (Patterson and Turner, 1997) which included 4 dioxin-like coplanar PCBs, 3) the data represent a wide range of adult ages, from 20 to over 70 years of age, and 4) the sampling was of relatively recent origin - 1995 to 1997, more recent than other studies reviewed in this chapter. Prior to describing this overall profile, information on four of the six study sites have been made available to EPA, and these will be described first.

With the assistance of the Agency for Toxic Substances and Disease Registry, the Missouri Department of Health (MDOH, 1999) conducted an exposure study to evaluate the potential impact of incinerating contaminated soil from Times Beach. Approximately 265,000 tons of soil and other materials containing 2,3,7,8-TCDD from 27 eastern Missouri sites were burned at the Times Beach Superfund site during the period March 17, 1996 through June 20, 1997. MDOH (1999) undertook a study to evaluate the impact of emissions from this incineration. Their approach was to take blood samples from a target and a comparison

population before, during, and after the incineration, and evaluate the differences in blood levels of dioxin-like compounds between the populations and over time. MDOH (1999) selected a target population based on air dispersion and deposition modeling. This population resided within a 4-kilometer radius of the incinerator. A comparison population from Manchester was located about 16 kilometers from the incinerator. From a list of over 650 individuals from both populations, totals of 76 and 74 individuals were selected from the target and comparison groups, respectively, for blood sampling. These selections considered demography, whether or not a woman was pregnant or breast feeding (neither was selected), and other critical factors. Blood samples were taken from all participants in September 1995, July 1996, and June 1997, and questionnaires were administered each time. Mean concentrations of each of 15 dioxin and furan congeners, and 4 coplanar PCB congeners were determined assuming non-detects were equal to one-half the detection limit. These detection limits, on a lipid basis, were: 0.8 ppt for the tetra- and penta-CDD congeners and the tetra- through octa-CDF congeners, 1.2 ppt for the hexa- through hepta-CDD congeners, 3.8 ppt for the coplanar PCB congeners, and 15.4 ppt for OCDD. Concentrations for two hexa-CDD congeners, 1,2,3,4,7,8-HxCDD and 1,2,3,6,7,8-HxCDD, and one hexa-CDF congener, 1,2,3,7,8,9-HxCDF, were not reported, and concentrations of one hepta-CDD congener which is not assigned a TEF value, 1,2,3,4,6,7,9-HpCDD, was reported. The mean concentrations for each congener for each testing period and study group, is shown in Table 4-6. Further details on this study can be found in MDOH (1999).

The CDC compilation included only the data from 1997. For that year, 67 of the 76 individuals from Times Beach had available measurements for their compilation, and 61 of the 74 individuals from the comparison site, Manchester, had available measurements.

MDOH (1999) concluded that there was no statistically significant differences between the target and comparison groups for all the analytes measured except for PCB 126, which was slightly higher in the comparison group. MDOH (1999) concluded that the values measured were some of the lowest values ever recorded on a human population. As seen in Table 4-6, the TEQ_{DFP}-WHO_{98} for the target group was 11.7 ppt while for the comparison group it was 12.6 ppt (averaged over all sampling dates). However, the actual TEQ concentrations would be higher than these since this study did not report on measurements for the three congeners noted earlier. Other data suggest that the hexa-CDD congeners not reported on in this study, mainly 1,2,3,6,7,8-HxCDD, comprise in the range of one-fourth to one-third of the

total body burden of TEQ. MDOH (1999) also observed that there appeared to be a decrease in concentrations from pre- to post-incineration for most analytes. Of all factors examined through questionnaires, only two appeared to be important for dioxin body burdens: smoking and age. Combining both populations, the average TEQ for participants living in homes with cigarette smokers as 12.8 ppt ($I\text{-}TEQ_{DF} + TEQ_{P}\text{-}WHO_{94}$), compared to 9.4 ppt ($I\text{-}TEQ_{DF} + TEQ_{P}\text{-}WHO_{94}$) in homes that do not have smokers. No age-specific results were presented in MDOH (1999), but a Pearson correlation of 0.525 for average TEQ concentration (statistical significance <0.001, two-tailed) was found for age. The average age of participants in both populations was about 43 years.

The Arkansas Department of Health (ADH) and the Agency for Toxic Substances and Disease Registry (ATSDR) cooperated on the design and implementation of a study to evaluate the exposure of individuals to dioxin-like compounds and other contaminants manufactured and then disposed of through incineration at the Vertac/Hercules Superfund Site (abbreviated the Vertac Site) in Jacksonville, Arkansas (ADH, 1995). The site had been used from the 1950s to manufacture herbicides such as 2,4,-D, 2,4,5-T, and 2,4,5-TP. It had changed hands several times until being abandoned by Vertac in 1987. Incineration occurred between 1992 and 1994. One component of the study was to sample and then analyze blood from three target groups of individuals: 1) residents living near the Site for more than 15 years as of 1991 - 72 individuals recruited, 2) residents living between 1 and 5 years as of 1991 - 36 recruited, and 3) residents living in a comparison area - 72 recruited; 71 participated. The comparison area chosen was in Mabelvale, Arkansas, a demographically similar community approximately 25 miles south of Jacksonville. Study participants ranged in age from 18 to 65 years old. The average age of the comparison group at the first sampling in 1991 was 40 years. Blood samples were taken in March, 1991, and participants also filled out an extensive questionnaire at that time. Subsets of individuals from all three populations were sampled once again in 1994 and 1995 after the incineration had been completed.

The CDC compilation used only the data from 1995 in their compilation. This data set included individuals who lived both in Jacksonville and in Mabelville - most of the individuals followed into 1995 lived in Jacksonville. The number of individuals sampled in 1995 included in the CDC compilation is 57.

The 1991 and 1994 sampling were described in a draft report released by the Arkansas Department of Health for public comment in 1995 (ADH, 1995). This report has never been

finalized. However, the blood data has been available and even used by one researcher citing results from the Mabelville population sampled in 1991 as a comparison group to his own study of dioxin-like compounds in the blood of a Great Lakes sport-fishing population (Anderson et al., 1998). Individual results that are summarized here have been provided to EPA via personal communication (Cranmer, 1996). The data supplied for each dioxin-like congener was either: identified as a quantified concentration (in serum, on a lipid basis), identified as "not detected" (ND), or identified as "not reported"(NR). Detection limits were not specified. Therefore, for purposes of the calculation of means, non-detects were assumed equal to zero. Measurements identified as NR were not included in the calculation of means.

Table 4-7 summarizes the results from the comparison population only. This table shows the results for the entire set of 71 individuals sampled in 1991. It also shows the results for subsets of these individuals that were sampled in 1994 and 1995. For comparison, the 1991 means for these same subsets are also provided. Unlike the target population of the Times Beach study described earlier, there appeared to be measurable impacts on the blood levels of dioxin-like compounds in the target populations at Vertac, as evidenced by the 1991 sampling. However, these impacts have not been tied directly to activities at Vertac. For example, in groups 1 (15 years residence near the site) and 2 (between 1 and 5 years residence), the mean lipid-based concentrations of 2,3,7,8-TCDD were 8.5 and 4.2 ppt, while the mean for the background population was 2.5 ppt. The high means for groups 1 and 2 were driven by a small number of very high concentrations (the three high concentrations from group 1 were 29.7, 84.9, and 94.8 ppt). However, if these high values are excluded, the overall concentrations from these groups are still higher than for the comparison group. The average TEQ_{DFP}-WHO_{98} from the comparison population in 1991 was 25.2 ppt. The select group of 18 individuals who were targeted for resampling in 1994 were individuals whose lipid-based concentration of 2,3,7,8-TCDD ranged from 2 to 5 ppt. Table 4-7 suggests that the average blood TEQ_{DFP}-WHO_{98} level for this group decreased between 1991 and 1994, from 26.8 to 22.6 ppt. However, when evaluating the average CDD/CDF/PCB concentration of the 14 individuals resampled in 1995 (a further subset of the 18 who provided samples in 1994), there appears to be little evidence of a decline in TEQ_{DFP}-WHO_{98}. The TEQ_{DFP}-WHO_{98} concentrations were 25.0 ppt in 1991 and 24.0 ppt in 1995 for this group. As with other studies, ADH (1995) also reported on an important age effect - the levels of dioxins and furans increased with age.

Grassman et al. (1999) developed a method to evaluate inter-individual variation in dioxin responsiveness among humans. Specifically, they developed a system that measures dioxin-responsive biomarkers in peripheral blood lymphocytes challenged *in vitro* with 10 nM TCDD during cell culture. Grassman et al. (1999) evaluated the capabilities of this method by obtaining blood samples from 3 populations widely variable in the magnitude and duration of their exposure to dioxin. One was a group of plant workers in a German chemical manufacturing plant, one was comprised of men, women, and children living in the vicinity of Seveso, Italy, during the accidental release of 2,3,7,8-TCDD in 1976, and the third was comprised of adult North Carolina volunteers, with no known occupational or unusual exposures to dioxin. This third group is comprised of 29 individuals, with ages ranging from 21 to 52 years, mean of 34.5 years, and it is the results from their analyses that are considered here as a U.S. background population. Grassman et al. (1999) reported that their average lipid-based TEQ_{DFP}-WHO_{94} was 14.2 ppt. Results of the study comparing the three study groups are reported in Grassman et al. (1999).

The North Carolina participants were sampled in 1996. EPA was provided the congener specific data for the 29 individuals of this study (Masten, 2000). Average congener concentrations from this group are provided in Table 4-8. Interferences were found in the analysis for 1,2,3,6,7,8-HxCDD, so this congener was not reported for any of the individuals, and TEQs were calculated without this congener. Other body burden data suggests that this congener could comprise in the range of one-fourth to one-third of the body burden of TEQ_{DFP}, so the overall TEQ for this population is underestimated. A small number of additional measurements from other congeners were not reported, and these were not considered in the generation of mean congener values. The mean values were calculated by assuming that non-detects were equal to one-half the detection limit. With this procedure, the lipid-based TEQ_{DFP}-WHO_{98} was calculated to be 15.0 ppt. Assuming that non-detects are equal to zero would not change these results by much; the lipid-based TEQ_{DFP}-WHO_{98} in this case was calculated as 13.0 ppt.

The CDC compilation includes these same data from the 29 North Carolina individuals.

The congener profile for the overall compilation done by CDC is shown in Table 4-9. These averages were derived assuming non-detects were equal to ½ the detection limit. These average congener concentrations were derived only using data from the overall set where these congeners were reported. As noted in the above discussions, there were some

studies where congeners were not reported, such as 1,2,3,6,7,8-HxCDD. Therefore, the number of observations that went into calculating overall averages for each congener was less than or equal to the total number of individuals (n = 316) in the study. These congener profiles were not used to generate TEQ concentrations for the overall data base. Instead, Patterson (2000) supplied statistical results for the TEQ_{DFP}-WHO_{98} concentrations that were generated using substitution methods for each individual included who had "not reported" (NR) for some of the congeners. Each time a congener was NR in an individual's congener profile, the average concentration from other individuals in the same study set was substituted for the individual who had the missing data. When that congener was missing from an entire study set, then the average for that congener from all other data sets where it was reported was substituted for all individuals in the data set with the missing congener. With these substitution techniques, every individual included in the overall data base had a complete set of congener results including quantified concentrations, non-detects with known detection limits, and substituted values. Then, each individual's TEQ_{DFP}-WHO_{98} lipid-based concentration was derived (assuming non-detects equal ½ detection limit), and from these TEQs, means and percentiles were generated. By this discussion, it should be clear that one cannot derive the TEQ concentrations In Table 4-9 from the congener profiles in Table 4-9, although they will be close.

As seen in Table 4-9, the average lipid-based TEQ_{DFP}-WHO_{98} concentration was 22.1 ppt. It was found that the substituting ND = ½ LOD did not influence the TEQ results. At ND = 0, the average TEQ concentration was only 1 ppt lower at 21.1 ppt TEQ_{DFP}-$WHO_{98.}$ However, this TEQ_{DFP}-WHO_{98} concentration included only 4 of the 12 coplanar PCB congeners. The overall compilation of literature data on coplanar PCB concentrations in human tissues, other than this CDC compilation, shown in Table 4-20, includes data on 11 of the dioxin-like coplanar PCBs. That data suggests a weighted mean TEQ_{P}-WHO_{98} concentration in blood of 15.6 ppt TEQ_{P}-WHO_{98}, of which these four congeners comprise 5.9 ppt. Therefore, the congeners missing from the CDC data base account for 62% [(15.6-5.9)/15.6 * 100%] of the total PCB TEQ estimated in the early 1990's for blood. From the congener profile in Table 4-9, it is calculated that the 4 PCB congeners add about 2.0 ppt TEQ to the overall mean concentration of 22.1 ppt. Assuming that the missing congeners from the CDC study data contribute the same proportion to the total PCB TEQ as in earlier data, they would increase the estimate of current PCB blood concentrations by another 3.3 ppt TEQ_{P}-WHO_{98} lipid for a total PCB TEQ of

5.3 pg/g lipid and a total TEQ_{DFP}-WHO_{98} of 25.4 ppt lipid. This will be the TEQ lipid concentration assumed to represent current background conditions in the United States.

In summary, the CDC data base includes 316 individuals from 6 sites in the time frame of 1995-1997. The mean TEQ tissue level from the study data alone is 22.1 ppt TEQ_{DFP}-WHO_{98}. Because this concentration does not include important dioxin-like PCB congeners, this average has been increased to 25.4 ppt TEQ_P-WHO_{98} using information from earlier studies of dioxin-like PCBs in blood, and this concentration will be used to represent current background conditions in the United States. This use includes an overall conclusion for body burdens of dioxin-like compounds in this chapter, as well as an assumption for mother's milk concentration in an evaluation of the impacts of nursing on infants in Chapter 5.

It is important to note that the 95th percentile concentration from this study data base is 38.8 ppt TEQ_P-WHO_{98}, which is nearly twice the mean from this study of 22.1 ppt TEQ_P-WHO_{98}. Later in this chapter, variation in background dose is investigated using data on dietary consumption of fats. There, using statistical surveys on food consumption, it was found that the 95th percentile of fat consumption was about twice the mean (and the 99th percentile is about 3 times the mean). Knowing that dioxins are transmitted primarily through consumption of dietary fat, this result from the CDC blood compilation is very consistent with the diet result - the 95th percentile consumption of dietary fat would appear to lead to the 95th percentile in body burden of dioxin-like compounds.

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Table 4-6. Mean Concentrations of CDD/CDFs and Coplanar PCB Congeners from the Times Beach Exposure Study

	Target Population (n=76)					Comparison Population (n=74)				
	Sep, 1995	July, 1996	June, 1997	Mean	n*	Sep, 1995	July, 1996	June, 1997	Mean	n*
CDD Congeners										
2,3,7,8-TCDD	1.79	1.27	1.23	1.43	66	1.46	1.38	1.23	1.36	61
1,2,3,7,8-PCDD	4.93	4.04	2.95	3.97	67	4.53	4.96	3.45	4.31	60
1,2,3,7,8,9-HxCDD	7.24	5.98	5.15	6.12	64	6.28	7.25	5.47	6.33	59
1,2,3,4,6,7,8-HpCDD	88.0	75.4	60.5	74.6	60	83.7	84.7	64.8	77.8	61
1,2,3,4,6,7,9-HpCDD	0.89	1.06	0.68	0.88	58	0.99	0.93	0.79	0.90	59
OCDD	650.0	542.0	435.0	542.3	64	535.0	512.0	404.0	483.7	46
TEQ_D-WHO_{98}	8.4	6.7	5.3	6.8		7.5	8.0	5.9	7.1	
CDF Congeners										
2,3,7,8-TCDF	0.48	0.56	0.53	0.52	62	0.56	0.54	0.45	0.52	51
1,2,3,7,8-PCDF	0.42	0.46	0.46	0.45	66	0.48	0.49	0.46	0.48	60
2,3,4,7,8-PCDF	5.73	5.00	4.12	4.95	61	5.43	5.82	4.52	5.26	59
1,2,3,4,7,8-HxCDF	7.36	6.40	5.03	6.26	64	6.18	7.24	4.91	6.11	59
1,2,3,6,7,8-HxCDF	6.40	5.07	4.01	5.16	65	5.19	5.86	4.03	5.03	58
2,3,4,67,8-HxCDF	0.46	0.45	0.47	0.46	63	0.77	0.80	0.63	0.73	55
1,2,3,4,6,7,8-HpCDF	14.4	12.1	9.0	11.83	63	11.5	11.7	8.30	10.5	59
1,2,3,4,7,8,9-HpCDF	0.40	0.47	0.42	0.43	65	0.45	0.42	0.40	0.42	58
OCDF	1.13	1.08	0.56	0.92	53	1.22	1.08	1.46	1.25	48
TEQ_F-WHO_{98}	4.5	3.9	3.2	3.9		4.1	4.5	3.4	4.0	
Coplanar PCB Congeners										
77	2.43	1.90	2.52	2.28	63	1.90	2.47	2.22	2.20	59
81	1.97	1.92	1.91	1.93	65	2.13	2.10	2.07	2.10	54
126	9.97	8.80	8.15	8.97	66	12.8	14.2	12.3	13.1	59
169	16.4	14.4	10.8	13.9	63	16.2	16.4	13.1	15.2	59
WHO_{98} TEQ_P	1.2	1.0	0.9	1.0		1.4	1.6	1.4	1.5	

* n = number of individuals with measurements of this congener for all three sampling dates.

Source: MDOH (1999).

Table 4-7. Results of Blood Sampling for the Comparison Population at Vertac in Jacksonville, AK

	1991 Sampling of 71 individuals	1994 Resampling of 18 individuals		1995 Resampling of 14 individuals	
	1991	1991	1994	1991	1995
CDD Congeners					
2,3,7,8-TCDD	2.5	3.0	2.7	3.1	3.3
1,2,3,7,8-PCDD	6.1	6.6	5.7	5.9	5.9
1,2,3,4,7,8-HxCDD	7.7	7.9	12.4	7.4	NR
1,2,3,6,7,8-HxCDD	70.8	70.4	56.0	66.4	68.1
1,2,3,7,8,9-HxCDD	8.6	8.9	7.2	9.8	10.2
1,2,3,4,6,7,8-HpCDD	124.1	115.0	77.2	102.9	81.7
OCDD	970.8	944.7	608.7	690.6	650.9
TEQ_D- WHO_{98}	18.6	19.6	16.8	18.4	17.9
CDF Congeners					
2,3,7,8-TCDF	2.0	0.6	0.2	0.6	0.1
1,2,3,7,8-PCDF	0.1	0.3	0 (ND)	0.2	0 (ND)
2,3,4,7,8-PCDF	5.4	6.4	5.6	5.9	5.6
1,2,3,4,7,8-HxCDF	8.1	8.0	6.8	7.4	6.6
1,2,3,6,7,8-HxCDF	5.0	5.6	4.4	5.1	4.9
1,2,3,7,8,9-HpCDF	0 (ND)	0 (ND)	0 (ND)	0 (ND)	0 (ND)
2,3,4,6,7,8-HxCDF	3.2	4.0	2.6	4.0	2.5
1,2,3,4,6,7,8-HpCDF	19.9	18.0	13.5	18.9	14.6
1,2,3,4,7,8,9-HpCDF	0.1	0.3	0.2	0 (ND)	0 (ND)
OCDF	0.6	0.8	0 (ND)	1.0	0 (ND)
TEQ_F-WHO_{98}	4.7	5.2	4.3	4.9	4.4
Coplanar PCB Congeners					
77	5.9	3.1	0 (ND)	4.4	NR
81	0 (ND)	0 (ND)	0 (ND)	0 (ND)	0.4
126	17.2	17.6	13.2	15.4	15.1
169	16.3	20.8	18.5	18.2	17.9
WHO_{98} TEQ_P	1.9	2.0	1.5	1.7	1.7

Source: ADH (1995) and Cranmer (1996).

Table 4-8. Congener-specific Average Concentrations for 29 North Carolina Adults

	North Carolina Adults, n=29, sampled in 1996
CDD Congeners	
2,3,7,8-TCDD	2.38
1,2,3,7,8-PCDD	4.51
1,2,3,4,7,8-HxCDD	3.46
1,2,3,7,8,9-HxCDD	3.99
1,2,3,4,6,7,8-HpCDD	54.04
OCDD	391.3
TEQ_D-WHO_{98}	8.22
CDF Congeners	
2,3,7,8-TCDF	1.01
1,2,3,7,8-PCDF	1.16
2,3,4,7,8-PCDF	6.26
1,2,3,4,7,8-HxCDF	5.44
1,2,3,6,7,8-HxCDF	4.67
2,3,4,6,7,8-HxCDF	1.66
1,2,3,7,8,9-HxCDF	1.37
1,2,3,4,6,7,8-HpCDF	11.77
1,2,3,4,7,8,9-HpCDF	1.32
OCDF	2.80
TEQ_F-WHO_{98}	4.74
Coplanar PCB Congeners	
77*	51.00
81*	4.11
126*	17.95
169*	14.95
WHO_{98} TEQ_P	2.00

* PCBs 77 and 81 were not detected in any sample, so the concentrations shown are the average of ½ detection limit for the 29 samples. PCBs 126 and 169 were detected in most of the samples, so the average concentrations calculated at ½ detection limits reported above are very similar to average concentrations calculated at ND = 0.

Source: Masten (2000).

Table 4-9. Results of CDC compilation of blood data from six study sites (all results in pg/g lipid; n = 316)

Congener	Mean	75th Percentile	90th Percentile	95th Percentile
CDD Congeners				
2,3,7,8-TCDD	2.1	2.7	3.5	4.2
1,2,3,7,8-PCDD	5.2	6.5	7.8	9.2
1,2,3,4,7,8-HxCDD	6.2	7.8	10.9	12.0
1,2,3,6,7,8-HxCDD	73.1	87.6	116.9	127.3
1,2,3,7,8,9-HxCDD	7.1	8.8	10.7	12.6
1,2,3,4,6,7,8-HpCDD	79.2	94.9	131.3	161.5
OCDD	664.0	793.6	1084.7	1394.0
CDF Congeners				
2,3,7,8-TCDF	0.7	0.9	1.2	1.5
1,2,3,7,8-PCDF	0.8	1.0	1.4	1.7
2,3,4,7,8-PCDF	6.2	7.5	10.2	12.2
1,2,3,4,7,8-HxCDF	6.5	7.8	10.5	12.2
1,2,3,6,7,8-HxCDF	5.3	6.2	8.4	9.8
1,2,3,7,8,9-HpCDF	0.7	0.8	1.2	1.4
2,3,4,6,7,8-HxCDF	2.2	2.6	3.3	4.0
1,2,3,4,6,7,8-HpCDF	13.2	15.4	21.2	25.8
1,2,3,4,7,8,9-HpCDF	1.3	1.5	2.1	2.6
OCDF	2.1	2.6	3.3	4.0
Coplanar PCB Congeners				
77	31.1	32.6	51.7	72.7
81	3.2	3.9	5.4	6.9
126	18.1	21.8	32.2	45.8
169	19.4	25.1	32.7	37.7
Toxic Equivalent Concentrations for the Entire Data Base*				
TEQ_{DFP}-WHO_{98}	22.1	26.7	33.9	38.8

* This TEQ concentration was derived separately from the congener profile, and cannot be derived from the profile. See text for more detail.

The following subsection will appear in Volume III. Properties, Environmental Levels, and Background Exposures, and will replace the current section 5.2. of Chapter 5, Nursing Infants. Other references to the findings in Section 5.2. throughout Chapter 5 and Volume III will need to be updated based on the information in this revised section.

5.2. NURSING INFANTS

Nursing infants may be exposed to dioxin-like compounds via consumption of breast milk. These compounds are deposited in the fatty tissues (i.e., adipose tissue, blood lipids, and breast milk) of the mother and may be transferred to the infant during nursing. Based on data from 1989, approximately 52 percent of U.S. mothers initiate breastfeeding with their newborn infants, and 40 percent continue breastfeeding for 3 months or longer (NAS, 1991). At 5 to 6 months of age, only about 20 percent of infants are breast-fed (NAS, 1991). This section will show how breast milk ingestion exposures, which are higher during breast-feeding, on a body weight basis, than during any other period in an individual's life, impacts lifetime exposures and body burdens. First, data showing the impact of breast milk ingestion to the infant body burden of CDD/CDF/PCBs are reviewed. Then, an estimate of the dose (average daily dose, ADD, and lifetime average daily dose, LADD) to the infant via breast milk is made. The section will close by developing, testing, and applying a model on the impact of breast-feeding to body burdens for growing infants.

5.2.1. The Impact of Breast Feeding on Infant Body Burden

Abraham et al. (1994, 1995) studied CDD/CDF/PCB levels in the blood of a breast-fed and a formula-fed infant at 11 and 25 months of age. Sampling of blood showed that the body burden of dioxin-like compounds was more than an order of magnitude higher for the breast-fed infant than the formula-fed infant during both time periods, with CDD/CDF ranging from 34.7 (11 months) to 43.9 (25 months) ppt TEQ_{DF}-WHO_{98} lipid-basis in the breast-fed infant compared to 2.7 to 3.3 ppt TEQ_{DF}-WHO_{98} for the formula-fed infant. Dioxin-like PCB concentrations were similarly an order of magnitude different, with the breast-fed infant having a concentration of 31.4 ppt TEQ_{P}-WHO_{98}, compared to 2.5 ppt TEQ_{P}-WHO_{98} for the formula-fed infant at 11 months (PCB 126 not measured at 25 months, so a comparison for that age is not informative). The full congener profiles for these results are shown in Table 5-1. The increase in the lipid-based CDD/CDF TEQ concentration in the blood of the breast-fed infant at

25 months was attributed to the relative decrease in body fat mass during the period between sampling and slight increases in body burden concentrations.

Abraham, et al. (1994) also analyzed mother's milk at 1 month and mother's blood along with the infants' blood at 11 months. They found mother's milk to contain 23.5 ppt TEQ_{DF}-WHO_{98} at 1 month and mother's blood to contain 14.2 ppt TEQ_{DF}-WHO_{98} at 10 months. If blood and milk concentrations in a mother during lactation are the same at any given time, then this data suggests a reduction of about 40% in TEQ concentration in the mother between the 1st and 10th month of lactation. The reduction in mother's milk concentration of dioxins during nursing is discussed further in Section 5.2.3 below.

Kreuzer, et al. (1997) developed and tested a toxicokinetic model of human lifetime body burden of TCDD, starting with a model for breast-feeding. To support their model, they presented adipose tissue and liver data on 3 stillborn and 17 infants who had died from sudden infant death syndrome (SIDS). Nine of the 17 infants had spent some portion of their young lives in breast-feeding, while the other 8 infants were formula-fed. Average congener and TEQ concentrations for these three groups are shown in Table 5-2. As seen, the highest TEQ concentrations are found in the infants who had some breast-feeding, with adipose concentrations at 15.9 ppt TEQ_{DF}-WHO_{98}, as compared to formula-fed infants who had concentrations at 4.3 ppt TEQ_{DF}-WHO_{98}. The breast-fed infants concentrations included four infants who were weaned several weeks prior to their death from SIDS. This may have generally led to reductions in their body burdens as their higher daily intake from breast-feeding was reduced after weaning. The average TEQ concentration for the five infants who died while still breast-feeding was 20.1 ppt TEQ_{DF}-WHO_{98}. The highest concentration found was for the infant who was breast-fed the longest at 19 weeks, and who died at that time; the TEQ concentration was 35 ppt TEQ_{DF}-WHO_{98}. Other breast-fed infants, however, did not have as much impact - infants who died while breast-feeding at 12 and 16 weeks had concentrations at 9 and 7.5 ppt TEQ_{DF}-WHO_{98}. While Kreuzer, et al. (1997) concluded that breast-fed infants had concentrations elevated as compared to formula-fed infants, they also observed that breast-fed infants had adipose TEQ concentrations that were within the range or lower than the values published for adults.

Patandin, et al. (1997) looked at the plasma levels of four polychlorinated biphenyls (PCBs) in 173 Dutch children 3.5 years of age, 91 of which had been breast-fed and 82 formula-fed. Children in the breast-fed group had significantly higher median PCB levels in

plasma ($p<0.0001$) than children in the formula fed group. The four PCBs measured were 118, 138, 153, and 180. The median sums of these four PCBs in the two groups of children were 0.750 µg/L in the breast-fed group versus 0.210 µg/L in the formula fed group. By means of an extensive questionnaire on dietary history combined data on concentrations of dioxin and PCBs provided by the Dutch National Institute of Public Health and the Environment, they were able to determine that the TEQ intake via the diet was virtually indistinguishable in the two groups. They found that PCB levels in the breast-fed children were significantly correlated with the period of breast-feeding ($r=0.63$), milk PCB levels ($r=0.39$), and the total TEQ in breast milk ($r=0.36$). They concluded the place PCB levels in Dutch children are the result of exposure through breast milk and in utero exposure, and that the influence of dietary intake of PCBs after weaning is small compared to the intake during breast-feeding.

5.2.2. Calculation of an Average Daily Dose from Breast-Feeding

Using the estimated dioxin concentration in breast milk, the dose to the infant can be estimated as follows:

$$ADD_{infant} = \frac{C_{milk\ fat} \cdot IR_{milk} \cdot ED \cdot f_3 \cdot f_4}{BW_{infant} \cdot AT} \qquad \text{(Eqn. 5-1)}$$

where,

ADD_{infant} = Average daily dose to the infant (pg/kg-d);
$C_{milk\ fat}$ = Concentration in milk fat (pg/g);
IR_{milk} = Ingestion rate of breast milk (kg/d);
ED = Exposure duration (yr);
BW_{infant} = Body weight of infant (kg);
AT = Averaging time (yr);
f_3 = Fraction of fat in breast milk; and
f_4 = Fraction of ingested contaminant that is absorbed.

This approach assumes that all pertinent parameters, including the body weight of the infant, the infant ingestion rate of breast milk, and perhaps most importantly, the contaminant concentration in milk, represent the average over the breast feeding time period.

Smith (1987) reported that a study in Britain found that the breast milk ingestion rate for 7- to 8-month old infants ranged from 677 to 922 mL/d and that a study in Houston measured the mean production of lactating women to range from 723 to 751 g/d. Smith (1987) also reported that breast milk ingestion rates remain relatively constant over an infant's life. For purposes of this section, a milk ingestion rate of 800 mL/d will be assumed. Smith (1987) also assumed that mother's milk has a 4 percent fat content, and that 90 percent of the ingested contaminant are absorbed. The infant weight varies with time. For example, a typical female infant weighs about 3.3 kg at birth, 7.3 kg at 6 months, and 9.2 kg at 1.0 year (Walker and Watkins, 1997).

The concentration of dioxin in the mother's milk is also expected to change, since lactation provides a significant avenue of depuration. Lakind, et al. (2000) cite several references where measurements of breast milk concentrations of lipophilic compounds (PCBs, DDE, DDT, CDD/CDFs) were shown to decline during the course of lactation. They fit available data on 2,3,7,8-TCDD to a curve, and their resulting relationship showed an 86% loss over 6 months. This is comparable to a modeling effort by Kreuzer et al. (1997), who modeled a 70% decline in TCDD concentrations after 6 months. Their model was more mechanistic and added the loss by breast milk to an overall female body burden model which included inputs by food consumption and outputs by metabolic and non-metabolic pathways. Patandin, et al. (1999), in their modeling of dioxin exposures from infancy to adulthood, cite data from Germany and England to conclude that breast milk concentrations of TCDD decline by 20% every 3 months. The data described in the previous section by Abraham, et al. (1994) suggest a decline of 40% of TEQs from 1 month to 10 months of lactation.

For assignment of $C_{milk\ fat}$ in Equation 5-1, therefore, one would have to assign a concentration at birth and consider a decline in that concentration over time. For purposes of this discussion, it is assumed that mother's milk concentration is 25 ppt TEQ_{DFP}-WHO_{98} lipid basis when lactation begins (which is the average tissue concentration derived from recent studies of dioxins in blood in background settings of the US, reviewed in Chapter 4). Then, it will be assumed to linearly drop by 50% after 6 months and an additional linear drop of 50% by the end of 12 months, for a total of a 75% decline from initial concentrations. These assignments in concentration decline are in the middle of the range reported above. They translate to concentrations of 12.5 ppt TEQ_{DFP}-WHO_{98} after 6 months and 6.3 ppt TEQ_{DFP}-WHO_{98} after a year, given a starting concentration of 25 ppt TEQ_{DFP}-WHO_{98}.

The proper way to derive an average dose to the child is to integrate Equation 5-1 over the time period of interest. At birth, for example, with a mother's milk concentration of 25 ppt TEQ_{DF}-WHO_{98}, an infant body weight of 3.3 kg, an average ingestion rate of 800 g/d breast milk, the dose is predicted to be 218 pg TEQ_{DF}-WHO_{98}/kg bw/day [(25 pg/g x 0.04 x 0.9 x 800 g/d) / (3.3 kg) = 218 pg/kg-d]. Using body weights and concentrations noted above, the dose at 6 months and 1 year would be 49 and 20 pg TEQ_{DF}-WHO_{98}/kg bw/day. Doing this calculation for each of the first twelve months of life and then dividing by12 results in an average dose to the infant of 77 pg TEQ_{DF}-WHO_{98}/kg bw/day.

This value is much higher than the estimated average background TEQ_{DFP}-WHO_{98} exposure to adults, 1 pg TEQ_{DFP}-WHO_{98}/kg-d. However, if a 70 year averaging time is used for this one-year nursing scenario, then the LADD (Lifetime Average Daily Dose, calculated as ADD * ED/LT where LT is lifetime typically assumed to be 70 years) is estimated to be 1.07 pg TEQ_{DFP}-WHO_{98}/kg-d ([77 pg/kg-d] * 1 yr/70 yr). This is essentially identical to the adult background exposure. However, this can be misleading since it ignores the difference in daily intake during potentially sensitive stages in development. Also, it doesn't consider any exposures past the first year of life. In order to calculate a true lifetime average daily dose, one needs to incorporate the changes in dose over various life stages. Using the estimates of dose derived in Chapter 4 for various ages in children: 1-5: 3.6 pg TEQ_{DFP}/kg-d, 6-11: 1.9 pg TEQ_{DFP}/kg-d, and 12-19: 1.1 pg TEQ_{DFP}/kg-d, the following calculates the LADD for lifetime background exposures considering one year of breast-feeding:

$$LADD = 77\ \frac{1yr}{70yrs} + 3.6\ \frac{4yrs}{70yrs} + 1.9\ \frac{6yrs}{70yrs} + 1.1\ \frac{8yrs}{70yrs} + 1.0\ \frac{51yrs}{70yrs}$$

$$LADD = 2.3\ \frac{pg\ TEQ_{DFP}}{kg-day}$$

On a mass basis, the cumulative dose to the infant after a year is about 188 ng TEQ (77 pg/kg-d x 6.7 kg x 365 d x ng/1,000 pg; 6.7 kg is an average annual weight based on the average of 12 monthly body weights). Using the age-dependent doses derived in Chapter 4, a dose from year 1 to year 70 in a 70-year lifetime calculates to 1644 ng TEQ_{DFP}-WHO_{98}, so that a total lifetime dose is 1832 ng TEQ_{DFP}-WHO_{98} (1644 + 188). This suggests that about 10% of

lifetime dose (188/1832 * 100%) may occur as a result of breast feeding, if that feeding occurred for one year.

5.2.3. Modeling the Impact of Breast-Feeding on Infant Body Burden

The previous section described an approach to estimate doses received by an infant due to breast-feeding, which included a starting concentration in mother's milk, a decline of that concentration over time (and the resulting decline in dose delivered to the child), and the child's changing body weight. That information will be used in this section to evaluate the impact of breast feeding on an infant's body burden of dioxins.

A one compartment non-steady state pharmacokinetic model is used to evaluate the effect of nursing on dioxin tissue levels. The model was based on the following differential equation describing the mass balance of dioxin in lipids (Pinsky and Lorber, 1998):

$$da(t)/dt = f\ D(t) - k(t)\ a(t) \qquad \text{Eqn. (5-2)}$$

$$c(t) = \frac{a(t)}{1000\ V(t)} \qquad \text{Eqn. (5-3)}$$

where:

a(t)	=	total mass of dioxins in lipid (pg) at time t
c(t)	=	concentration of dioxins in lipid (pg/g) a time t
D(t)	=	ingested dose of dioxins (pg/yr) at time t
V(t)	=	lipid weight (kg) at time t
k(t)	=	elimination rate constant (yrs^{-1}) at time t
t	=	time (yrs)
f	=	fraction of ingested dose absorbed into lipid compartment (unitless)

The previous section described the exposure dose during the first year of nursing. After nursing, the doses to the children are assumed to follow the regime described for different age ranges as described in Chapter 4. The lipid weight, V(t), is calculated as the product of the percent body lipid and the full body weight of the infant, both of which are provided in the

Walker and Watkins (1997) for infant boys and girls. This section will demonstrate the approach on infant girls. The dose regime for tested scenarios in this section, the body weight, lipid fraction, and subsequent lipid weight, are shown with other model parameters in Table 5-3.

The elimination rate constant, k(t), was developed in similar fashions by Pinsky and Lorber (1998), Michalek, et al. (1996), and Flesch-Janys, et al. (1996), for 2,3,7,8-TCDD. All three derived a relationship in which the elimination rate constant was a function of percent body fat. All three also curve-fit their empirical algorithms for k(t) on data from adult individuals, whose percent body fat was about 25%. With body fat percent increasing over time, particularly in older individuals, the elimination rate constant decreased (equivalently, the half-life increased) significantly. Given a range of body fat over time, from about a low of 15% to a high over 40% (for elderly females), the relationship in Pinsky and Lorber (1998) results in a half-life of 2,3,7,8-TCDD to range from about 6 to over 20 years.

None of these efforts, however, identifies processes or factors critical for infants, other than percent body fat. With body fat around 15% at birth, the half-life is calculated to be about 6.4 years using the relationship in Pinsky and Lorber (1998). Kreuzer, et al. (1997), however, develops a procedure for modeling the elimination half-lives for 2,3,7,8-TCDD which considers metabolic, t_m (breakdown by enzymes), and non-metabolic, t_f (fecal elimination) processes. These two half-lives were combined to solve for an overall half-life, $t_{1/2}$. Other key parameters included total body lipid mass and liver volumes, which change over time, and a reference half-life for an adult. For their “reference adult” at age 40, the cited an overall half-life of 5 years, based on information in Geyer, et al. (1986). Their model showed a rise in half-lives from a low less than 0.5 years at birth to a high of 5 years at the total body lipid mass of 20 kg. With their parameter assignments, perhaps most importantly this assignment of a 5 year half-life for a reference adult, the half-life will not go far beyond 5 years (as a function of body lipid mass, it would exceed 5 years when body lipid mass exceeds 20 kg), which makes the model of Kreuzer, et al. (1997) importantly different than that of Pinsky and Lorber (1998), Michalek, et al. (1996), and Flesch-Janys, et al. (1996), all of whom have half-lives varying from a value of 6 to over 20 years. In short, the model of Kreuzer, et al. (1997) has half-lives which mostly never exceed 5 years, while the other approaches have half-lives for TCDD which never go below 6 years.

As noted, the model of Kruezer, et al. (1997) suggests relatively short half-lives for infants. At that age, the overall half-life is driven by non-metabolic processes and the resulting half-life for newborns is calculated to be 0.42 years. It rises to about 2 years when the total body fat weight is about 5 kg, which will occur around ages 8-10 (25-35 kg overall body weight, about 20% body fat). Very clearly, this rapid a half-life of dioxin intake will have an important impact on the accumulation of dioxin residues during breast-feeding as compared to a model showing a 6 year or higher half-life. Lakind, et al. (2000) adopted Kruezer's approach in their evaluation of the impacts of breast-feeding on the 2,3,7,8-TCDD body burdens of infants.

For purposes of this assessment, it is assumed that the overall half-life for the early years of life will follow the model as derived by Kruezer, et al. (1997). After the first year of life, the half-life will be approximated as the mid-point between the low half-life of the Kreuzer model and the longer half-life derived as a percent of body fat in Pinsky and Lorber (1998). It is noted that had Kreuzer, et al. (1997) established reference half-lives for 40 year-olds more in the 6-20 year range, they would still have had very low half-lives at birth, rising to these higher half-lives with age. Their assignment of a metabolic half-life of 5 years is from Geyer, et al. (1986), and it is evaluated that the more recent work in the 1990s which places half-lives of TCDD at 7 years and higher based on percent body fat is more valid for the years after infancy. This remains an obvious uncertainty for this type of modeling approach. The final assumption for the model is the initial lipid concentration in the infant. It will be assumed to be10 ppt TEQ_{DFP}-WHO_{98}, reasonably similar to the 11.9 ppt TEQ_{DF}-WHO_{98} found in stillborn adipose tissue in Kreuzer, et al. (1997). The assumptions and parameter assignments for this modeling exercise, including the half-life change over time, are shown in Table 5-2.

It should be understood that the half-life algorithm of this exercise is very uncertain. No data could be found to collaborate the modeled half-life less than 1 year for infants. To this point, this is only a modeling approach.

However, it may be possible to test the overall model, including this half-life model, on measured data. Abraham, et al. (1994, 1995) provided concurrent data on mother's milk and infant blood concentrations of dioxin TEQs. As described in the above section, the mother's milk was sampled when the infant was one month old, and the concentration was 23.5 ppt TEQ_{DF}-WHO_{98}, lipid basis. The child was weaned at 10 months, and his blood was sampled at 11 months, with a resulting concentration of 34.7 ppt TEQ_{DF}-WHO_{98}, lipid basis. The model described in this section will be applied to this data as follows. The body weight and lipid

fraction monthly assignments for the infant as shown in Table 5-3 will be applied. The dose to the child is a function of the mother's milk concentration and assumptions of 800 g/d breast milk, 4% milk fat, and 90% absorption. This assumption of a 90% absorption for infants is supported by Lakind, et al. (2000), who selected a 95% absorption of 2,3,7,8-TCDD in a nursing model for TCDD and cited four studies showing this much absorption for the lower chlorinated dioxin compounds. Assuming 90% may be conservative for the higher chlorinated dioxins, which are shown to be excreted at a higher rate. As described earlier, the mother's milk concentration was measured to be 23.5 ppt TEQ_{DF}-WHO_{98}. Therefore, at birth, the dose is predicted to be 677 pg TEQ_{DF}-WHO_{98}/d [23.5 pg/g x 0.04 x 0.9 x 800 g/d = 677 pg/d]. Three scenarios will be tested. In the first, it will be assumed that the mother's milk concentration remains at 23.5 ppt for the duration of breast-feeding, and that the TEQs have a half-life of 7 years in the infant. This half-life assumption is typical for pharmacokinetic modeling of 2,3,7,8-TCDD, and consistent with the models described above which are based on a percent body fat. In the second, it will be assumed again that the concentration in the mother's milk remains constant, but that the half-life will vary as outlined in Table 5-3, essentially staying below 1 year for the first year of life. For the final test, the mother's milk concentration will be assumed to linearly decline by 50% over 6 months, and an additional 50% over the next six months, so that the dose drops to 339 pg TEQ/d after 6 months and to 170 pg TEQ/d after 1 year. The infant's lipid concentration predictions at 11 months are compared with the 34.7 ppt TEQ_{DF}-WHO_{98}, lipid basis, found by Abraham, et al. (1994). These predictions are:

	Concentration, ppt TEQ_{DF}-WHO_{98}, lipid
Scenario 1: 7 yr half-life, constant milk C	84
Scenario 2: half-life<1 yr, constant milk C	63
Scenario 3: half-life <1 yr, declining milk C	34

As seen, Scenario 3 matched the observed infant lipid concentration. At least for this data and simple test, it would appear that assumptions of declining milk concentrations and short half-lives in infants are important for accurately modeling the body burden of dioxin-like compounds in infants.

For the overall evaluation of the impact of breast-feeding on the infants body lipid concentrations of CDD/CDF/PCBs, four scenarios are modeled. Table 5-3 displays the assumptions for infant body weight, lipid fraction, and the assumed half-life for the

CDD/CDF/PCBs in the infants body. A clear uncertainty for this exercise is the use of an overall half-life derived for 2,3,7,8-TCDD (and still uncertain for TCDD) for CDD/CDF/PCB TEQ doses. Four dose scenarios are modeled. These include:

Scenario #1: Formula Only: In this scenario, the dose to the infant will be assumed to be 54 pg TEQ_{DFP}-WHO_{98}/d. This is the dose developed for the age range of 1-5, as described in Chapter 4. The dose by formula feeding may be lower or higher, as little information is available on the dioxin content of baby's formula. Doses from 6 to 11, 12 to 18, and greater than 18 years of age were 58, 63, and 70 pg TEQ_{DFP}-WHO_{98}/d, as developed for these age ranges in Chapter 4.

Scenario #2: Six-Week Nursing: The dose to the infant will be a function of the starting concentration of dioxins in the mother's milk, 25 pg TEQ_{DFP}-WHO_{98}/g lipid, and other assumptions that have been described in this section: 800 g/day milk ingestion, 4% lipids in milk, and 90% absorption by the child, resulting in an initial dose of 720 pg TEQ_{DFP}-WHO_{98}/d. This drops to 660 after 1 month, and then to 630 pg TEQ_{DFP}-WHO_{98}/d, when nursing stops. Doses from then are as in Scenario #1.

Scenario #3: Six-Month Nursing: The doses drop linearly from 720 to an ending concentration of 360 pg TEQ_{DFP}-WHO_{98}/g lipid at month 6. From there, doses are as in Scenario #1.

Scenario #4: The doses drop linearly from 720 to 360 at 6 months and then linearly again to 180 pg TEQ_{DFP}-WHO_{98}/g lipid at the end of one year. From there, doses again are as in Scenario #1.

The results from this exercise are shown in Figure 1, which shows the lipid concentrations and the body burdens from birth to 25 years of age. The body burden is simply calculated as the lipid concentrations times the lipid fraction. It is seen that the lipid concentrations rise to just above 40 ppt TEQ_{DFP}-WHO_{98} lipid for both the 6-month and the 1-year scenarios. Body burdens follow a similar trend, rising to about 9.5 ppt TEQ_{DF}-WHO_{98} for both the 6-month and 1-year scenarios. The body burdens decline as well for both these scenarios, but the decline is much slower for the nursing infant. The six-week scenario does show a rise in infant body burden to above 30 ppt TEQ_{DF}-WHO_{98}, but then a rapid drop tracking the formula-only scenario fairly well after about age 2. From Figure 1, it appears that all four scenarios begin to merge at about age 10. The rise in concentrations seen in the later

years in Figure 5-1 is due to the rise in body fat percent and the subsequent rise in half-life as predicted by elimination rate model of Pinsky and Lorber (1998).

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Table 5-1. Concentrations of CDDs, CDFs, and Dioxin-Like PCBs in Blood (lipid based) of a Breast-Fed and a Formula-Fed Infant at the Age of 11 and 25 Months

Compound (conc. in pg/g fat)	Age (Months)			
	Breast-Fed Infant		Formula-Fed Infant	
	11	25	11	25
2,3,7,8-T4CDF	<2.7*	<2.5	<3.0	<2.5
2,3,7,8-T4CDD	3.7	4.1	<1.0	<1.0
1,2,3,7,8-P5CDF	<1.2	n.d. (1.4)	<1.2	n.d. (2.5)
2,3,4,7,8-P5CDF	23.1	29.7	1.5	<2.5
1,2,3,7,8-P5CDD	11.1	15.2	<1.0	n.d. (1.8)
1,2,3,4,7,8H6CDF	9.8	12.2	<2.2	<2.5
1,2,3,6,7,8-H6CDF	8.1	10.2	<1.0	<2.5
2,3,4,6,7,8-H6CDF	<3.4	<3.0	<2.3	<2.5
1,2,3,4,7,8-H6CDD	7.8	9.1	n.d (1.1)	n.d. (2.8)
1,2,3,6,7,8-H6CDD	43.0	51.7	2.5	<5.4
1,2,3,7,8,9-H6CDD	7.1	8.1	n.d. (1.2)	<4.5
1,2,3,4,6,7,8-H7CDF	13.1	n.a.	<5.8	<6.0
1,2,3,4,6,7,8-H7CDD	24.3	29.7	8.8	<10.0
OCDF	<5.0	n.a.	<5.0	n.a.
OCDD	148.7	204.0	79.3	70.0
TEQ_{DF}-WHO_{98} (<LD=0.5*LD)	29.2	36.8	2.4	2.3
PCB 77	23 (m)	20 (m)	26 (m)	20 (m)
PCB 126	287	n.a.	24	n.a.
PCB 169	270	183	7	11
TEQ_{P}-WHO_{98}	31.4	1.8	7	0.1

* for values reported as "<" a value (2.7, e.g.), ½ the concentration was used for TEQ calculations.
n.a. = not analyzed
n.d. = not detected (limit of detection)
(m) = maximum value, due to possible contribution of a contaminant
Source: Abraham et al. (1995).

Table 5-2. Concentrations of CDDs and CDFs in Adipose Tissue (lipid based) of Stillborn, Formula-Fed, and Breast-Fed Infants

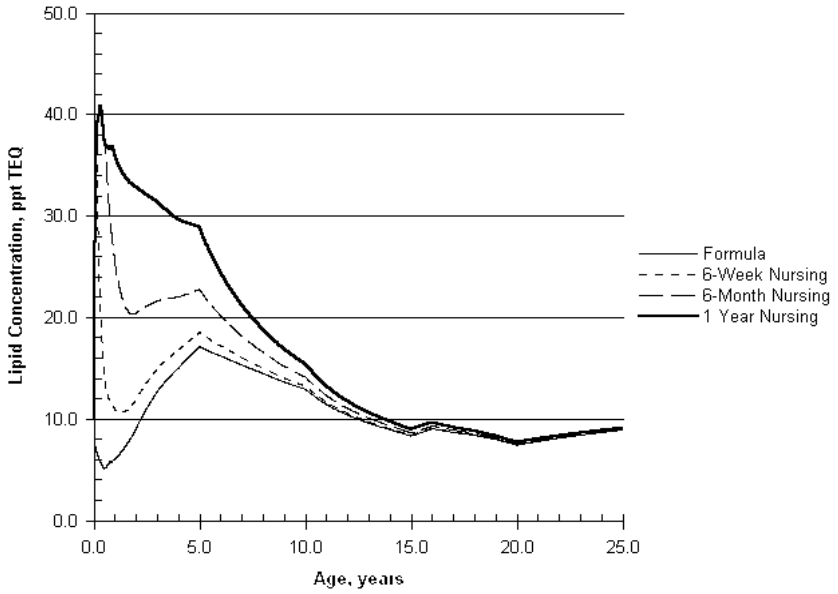
Compound (conc. in pg/g fat)	Stillborn (n=3)	Formula-Fed (n=8)	Breast-Fed (n=9)
2,3,7,8-TCDD	1.6	0.4	1.7
1,2,3,7,8-PCDD	3.4	1.1	4.9
1,2,3,4,7,8-HxCDD	2.5	1.0	4.0
1,2,3,6,7,8-HxCDD	8.8	4.0	19.9
1,2,3,7,8,9-HxCDD	1.3	0.7	3.7
1,2,3,4,6,7,8-HpCDD	12.9	5.0	25.2
OCDD	51.2	29.1	91.6
2,3,7,8-TCDF	1.4	1.9	1.1
1,2,3,7,8,-PCDF	0.2	1.0	0.5
2,3,4,7,8-PCDF	9.2	3.1	10.6
1,2,3,4,7,8-HxCDF	3.7	1.7	3.5
1,2,3,6,7,8-HxCDF	2.4	1.0	2.8
2,3,4,6,7,8-HxCDF	1.0	0.2	1.1
1,2,3,7,8,9-HxCDF	0.1	0.1	0.1
1,2,3,4,6,7,8-HpCDF	3.6	1.6	3.8
1,2,3,4,7,8,9-HpCDF	0.4	0.1	0.1
OCDF	2.1	1.8	1.6
TEQ_{DF}-WHO_{98}	11.9	4.3	15.9

Note: Average congener concentrations calculated assuming non-detects equal to ½ detection limit.

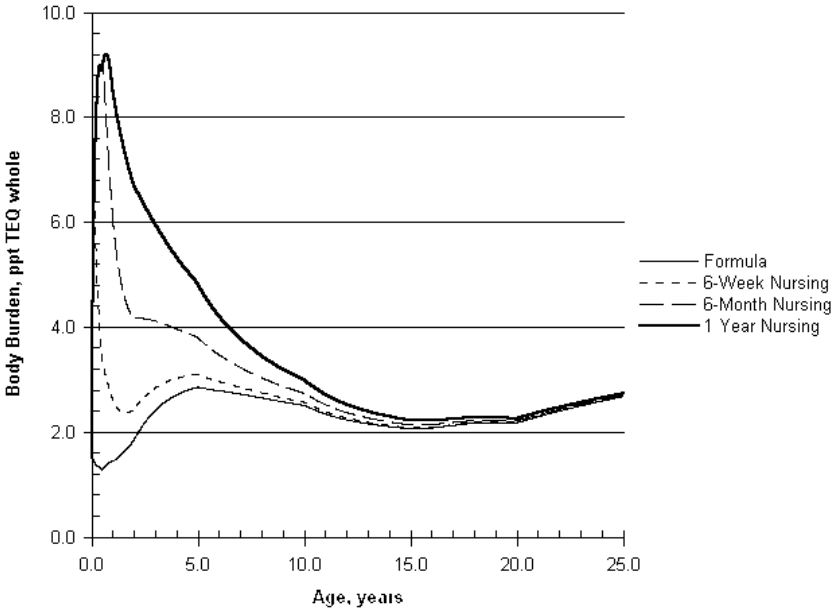
Source: Kreuzer, et al. (1997).

Table 5-3. Parameters used for the demonstration of the model for evaluating the impact of nursing from infancy to adulthood

Time after birth	Body Weight kg	Lipid Fraction	Half-life yrs	Dose of Dioxin TEQ_{DFP}- WHO_{98}, pg/day			
				formula only	6-week BF	6 months BF	1 year BF
At birth	3.3	0.15	0.52	54	720	720	720
1 month	3.9	0.17	0.57	54	660	660	660
2 months	4.6	0.22	0.63	54	630 / 54	600	600
3 months	5.3	0.23	0.70	54	54	540	540
4 months	5.9	0.24	0.78	54	54	480	480
5 months	6.6	0.25	0.86	54	54	420	420
6 months	7.3	0.25	0.95	54	54	360	360
7 months	7.6	0.25	0.97	54	54	54	330
8 months	7.9	0.25	0.98	54	54	54	300
9 months	8.2	0.24	0.97	54	54	54	270
10 months	8.5	0.24	1.00	54	54	54	240
11 months	8.8	0.24	1.01	54	54	54	210
1 year	9.2	0.24	1.03	54	54	54	180
2 years	11.9	0.20	2.00	54	54	54	54
5 years	17.7	0.17	4.00	58	58	58	58
11 years	37.1	0.20	5.20	63	63	63	63
18 years	58.0	0.26	6.60	70	70	70	70
25 years	64.0	0.30	7.50	70	70	70	70



(a)



(b)

Figure 5-1. Demonstration of the model for evaluating impacts on lipid concentrations (a) and body burdens (b) of infants resulting from various nursing scenarios.